DEPARTMENT OF HEALTH AND HUMAN SERVICES

and

CENTERS FOR DISEASE CONTROL AND PREVENTION

convene the

ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS

Atlanta, Georgia
June 23-24, 2004

RECORD OF THE PROCEEDINGS

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CENTERS FOR DISEASE CONTROL AND PREVENTION

ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
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Minutes of the Meeting

The Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) convened a meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on June 23-24, 2004 at CDC's Corporate Square Facility, Building 8, in Atlanta, Georgia.

Opening Session

Dr. Masae Kawamura, the ACET Chair, called the meeting to order at 8:31 a.m. on June 23, 2004. She welcomed the attendees to the proceedings and opened the floor for introductions. The following individuals were present for the deliberations.

ACET Members
Dr. Masae Kawamura, Chair
Dr. Michael Fleenor
Dr. David Gonzales
Ms. Harriett Gray
Ms. Sara Loaiza
Ms. Eileen Napolitano

***Ex Officio*s and Liaisons**
Ms. Duiona Baker (SAMHSA)
Dr. Amy Bloom (USAID)
Dr. Raymond Chinn (HICPAC)
Dr. Miguel Escobedo
(U.S.-Mexico BHC)
Dr. Fred Gordin (ATS)
Dr. Geralyn Johnson (DIHS)
Dr. Michael Kurilla (NIH/NIAID)
Dr. James McAuley (CCCS and IDSA)
Ms. Eva Moya (U.S.-Mexico BHC)
Ms. Tanya Oemig (NTCA)
Dr. Michael Puisis (NCCHC)
Dr. Gary Roselle (VA)
Ms. Rachel Stricof (APIC)
Dr. Michael Tapper (SHEA)
Dr. Theresa Watkins-Bryant (HRSA)

Designated Federal Official
Dr. Ronald Valdiserri,
Executive Secretary

CDC Representatives
Dr. Harold Jaffe
(Outgoing NCHSTP Director)

Dr. Janet Collins
(Acting NCHSTP Director)
Dr. Kenneth Castro, DTBE Director
Dr. Jeanne Bertolli
Mr. Mani Cherow
Ms. Ann Cronin
Ms. Thena Durham
Ms. Mollie Ergle (Contractor)
Ms. Paulette Ford-Knights
Ms. Judy Gibson
Dr. Stefan Goldberg
Dr. John Jereb
Mr. Nabeel Khan
Ms. Ann Lanner
Dr. Mark Lobato
Ms. Elizabeth Lowery
Dr. Susan Maloney
Ms. Lilia Manangan
Dr. Jerry Mazurek
Mr. Michael Melneck
Dr. Bess Miller
Dr. Thomas Navin
Ms. Anne O'Connor
Dr. Adelisa Panlilio
Mr. Paul Poppe
Mr. Joseph Scavotto
Ms. Margie Scott-Cseh
Dr. Andrew Vernon
Dr. Elsa Villarino
Dr. Wanda Walton

Guests
Dr. Christopher Coffey (NIOSH)
Dr. Jeff Hill (AHA and GHA)
Mr. John Seggerson (NCET)
Dr. Anthony Tran (APHL)

Dr. Ronald Valdiserri, the ACET Executive Secretary, informed the participants that ACET meetings are open to the public and all comments made during the proceedings are a matter of public record. He asked the members to be mindful of potential conflicts of interest identified by the CDC Office of Program Services and recuse themselves from voting or participating in these discussions.

Update by the National Center for HIV, STD and TB Prevention (NCHSTP) Acting Director

Dr. Janet Collins' report covered the following areas. First, Dr. Harold Jaffe, the outgoing NCHSTP Director, is retiring on June 30, 2004. The important contributions he made to the HIV, STD and TB fields during his impressive public health career were highlighted. The participants applauded Dr. Jaffe's outstanding accomplishments and strong leadership of NCHSTP and wished him well in his new position at the University of Oxford in England. A search will be conducted to identify the permanent NCHSTP Director. Other personnel changes in NCHSTP include a new Acting Associate Director for Science; Acting Associate Director for Management and Operations; and Acting Associate Director for Laboratory Services.

Second, the Division of AIDS, STD and TB Laboratory Research (DASTLR) will be dissolved and its four branches will be transferred to the NCHSTP Division of HIV/AIDS

Prevention, Division of STD Prevention (DSTDP), and Division of Tuberculosis Elimination (DTBE). The reorganization will become effective on July 19, 2004 and will strengthen integration among program focus areas, epidemiologic activities and laboratory research. Third, DSTDP and DTBE were evaluated in March 2004 under the Office of Management and Budget Program Assessment Rating Tool (PART). The evaluation is designed to systematically and clearly measure, diagnose and assess a program and its performance. Of the five CDC programs reviewed, DSTDP and DTBE received the highest scores. The PART scores will be final on June 30, 2004.

Fourth, CDC's new goals and organizational design in support of the Futures Initiative were recently announced in a May 2004 press release. The new structure will allow CDC to achieve a greater health impact; reduce health disparities for customers whose health CDC protects; lead the nation's public health system; expand public health research as the foundation for all CDC activities; expand the global impact; support the best workforce worldwide; and maximize effectiveness and accountability. The design was initiated by an "outside-in" approach in which input was extensively sought from federal agencies, customers and other partners. The most common theme that emerged from survey responses was the difficulty in understanding CDC's complex organization.

The most significant change is the integration of CDC's existing operational units into four new Coordinating Centers for Infectious Diseases; Health Promotion; Environmental Health, Injury Prevention and Occupational Health; and Health Information and Services. NCHSTP will be housed in the Coordinating Center for Infectious Diseases (CCID) along with the National Center for Infectious Diseases (NCID) and the National Immunization Program. The role of the coordinating center is still being defined, but efforts will be made to strengthen efficiency, integration and support across the three infectious disease centers. Dr. Mitchell Cohen has been appointed as the CCID Director. The Office of Global Health and Office of Terrorism Preparedness and Emergency Response (OTPER) will continue to be maintained as two separate units.

Other major changes are as follows. Two new National Centers for Health Marketing and Public Health Informatics will be established and housed in the Coordinating Center for Health Information and Services. The Epidemiology Program Office and Public Health Practice Program Office will be disbanded; specific divisions of these offices will be transferred to coordinating centers. Despite the new groupings within the coordinating centers, CDC has made an explicit commitment to maintain programmatic and scientific strengths of each individual national center. Dr. Julie Gerberding, the CDC Director, plans to finalize the organizational design by September 30, 2004.

Dr. Jaffe thanked DTBE for providing a forum for public health practitioners and clinicians to collaborate. He pointed out that this experience has been particularly rewarding for him. He also thanked ACET for serving as one of CDC's most useful and productive advisory committees and providing DTBE with solid guidance. The members commended Dr. Jaffe for his extensive involvement with and support of ACET during his tenure as the NCHSTP Director.

DTBE Director's Report

Dr. Kenneth Castro's report covered the following areas. Dr. Castro will serve on the transition team for the CDC reorganization to provide input on TB programs and activities that need to be protected and identify new opportunities for DTBE. Personnel changes include a new Clinical and Health Systems Research Branch Chief; a new Associate Director for Management and Operations; and the addition of 24 staff from DASTLR. DTBE participated in the American Lung Association/American Thoracic Society (ATS) 100th International Conference in May 2004.

The new project cycle for the TB cooperative agreements will begin in FY'05. In response to the changing TB epidemiology and anticipated level funding proposed in the President's budget request, DTBE has been extensively communicating with partners to identify the best process to redistribute funds. DTBE sponsored web-based seminars on March 3, April 29, June 2 and June 21, 2004 to facilitate discussion of the new funding cycle and obtain feedback from partners.

The Tuberculosis Epidemiologic Studies Consortium (TBESC) held a meeting in April 2004. The number of sites will be decreased in FY'05 from 22 to 16-18 due to DTBE's current and anticipated deficits in FY'04 and FY'05, respectively. DTBE and TBESC grantees discussed approaches to maintain capacity to conduct sound epidemiologic studies in light of the budget cuts. TBESC grantees will only focus on programmatically relevant research that will accelerate the TB decline, such as TB epidemiology in foreign-born persons and latent TB infection (LTBI).

The Tuberculosis Trials Consortium (TBTC) convened a meeting in May 2004 to review ongoing activities. Study 26 is an efficacy trial comparing a once-weekly course of isoniazid (INH)/rifapentine (RPT) and daily therapy of INH for 12 months. Of 8,000 participants needed for the study, ~3,000 have been enrolled to date. Study 27 is a Phase II trial evaluating the role of moxifloxacin in TB and early bactericidal activity. The addition of international TBTC sites has resulted in increased recruitment. Most notably, Study 27 is ahead of schedule due to the inclusion of the Uganda site. TBTC initiatives will be reduced due to budget cuts and one site has been permanently closed

based on poor recruitment. DTBE is currently developing objective evaluation and performance criteria to guide further funding decisions.

The National Tuberculosis Controllers Association (NTCA) convened a workshop in June 2004 focusing on the role of laboratories and the need to strengthen partnerships. Major agenda items and discussion topics included universal genotyping, rapid turnaround for TB test results, future laboratory needs in the face of decreased TB incidence, and efforts to maintain proficiency in low-incidence areas. Under contracts with California and Michigan laboratories, DTBE now has capacity to provide genotyping to TB patients. To date, 43 sites have submitted plans for universal or selected genotyping to enhance TB prevention and control.

The manufacturer of the second generation QuantiFERON-TB test (QFT-2g) has requested licensure from the Food and Drug Administration (FDA). DTBE held a consultation in June 2004 to evaluate recent data, discuss existing recommendations, and explore development of new guidelines when QFT-2g is licensed. DTBE will most likely provide technical assistance to FDA in assessing the manufacturer's licensure application and supporting data.

ACET was pleased that DTBE will be represented on the transition team for the CDC reorganization, but several concerns were expressed about the new structure. An advocacy organization recently circulated an e-mail alert announcing that CDC has been directed to eliminate its Office of Minority Health (OMH). This approach will further reduce federal support to minority populations for TB and other health disparities. Several local jurisdictions have pointed out that initiatives now being proposed in the reorganization may not be implemented if the current Administration changes and a new CDC Director is appointed.

The new design adds another layer of bureaucracy rather than streamlining CDC's current structure. For example, national center directors (NCDs) will report to coordinating center directors (CCDs) who will then communicate with the CDC Director. NCHSTP will no longer have the ability to directly convey TB funding needs and other priority issues to the CDC Director. Of the four new coordinating centers, OTPER is furthest away from CCID. This structure will decrease capacity of the three infectious disease centers to prepare for an event. Instead, OTPER should be closely aligned to CCID to strengthen the public health and healthcare infrastructures in responding to biological or chemical events.

Members of the Association of State and Territorial Health Officials and National Association of County and City Health Officials are concerned that the stronger focus on "customers" in the new organizational structure will compel CDC to abandon its traditional partnerships with state and local health departments. The reorganization

may further decrease the weak emphasis on TB. Current funding is only being allocated to control rather than eliminate TB; targeted testing dollars have been cut; and additional resources may not be provided to DTBE for training, education and communication to support the TB elimination effort. Moreover, the critically important role of public health laboratories in providing routine, clinical and diagnostic services may not be considered. This capacity must be maintained despite CDC's new organizational design because QFT-2g will shift the paradigm of diagnosing TB from clinicians to laboratories.

CDC addressed ACET's concerns with the following remarks. In general, CDC's deep commitment to health disparity issues should be strengthened in the reorganization. In particular, NCHSTP will contact the OMH Director to determine if a decision has been made on the placement of OMH in the new organizational structure. Outcomes from this discussion will be reported to ACET before the meeting is adjourned on the following day. A new CDC Director will not make dramatic changes to the new organizational structure that would minimize CDC's importance, damage productivity and progress, or harm capacity to respond to threats.

CCDs will not add another layer between NCDs and the CDC Director. NCDs will seek support from CCDs on funding requests, but will not be required to report to CCDs on the daily operation of the respective national center. Instead, the role of CCDs will be to enhance synergy, efficiency and integration across the national centers in each coordinating center. As the CCID Director, for example, Dr. Cohen would identify an NCHSTP activity that could assist the National Immunization Program. NCDs will still be able to directly communicate with the CDC Director after the coordinating centers are officially established.

Dr. Cohen's background as an infectious disease physician and tenure at CDC demonstrate his strong advocacy and support of TB and other infectious diseases. Of his 27 years at CDC, 15 have been as Director of the NCID Division of Bacterial and Mycotic Diseases. He served in this position when the TB laboratories were housed in the division. Moreover, he was extensively involved in development of the action plan to combat multi-drug resistant TB (MDR-TB). Dr. Cohen was unable to attend the present ACET meeting due to a scheduling conflict, but is expected to attend the next meeting.

NCHSTP shares ACET's concerns about the distance between CCID and OTPER, particularly since DTBE staff were detailed to bioterrorism activities during the anthrax and severe acute respiratory syndrome (SARS) outbreaks. This component of the new structure is still under discussion, but Dr. Cohen will be asked to vigorously pursue potential areas and programs where OTPER and NCHSTP can interface. The increased emphasis on "customers" in the new organizational design is designed to

strengthen CDC's impact on health outcomes and disparities of the public. To support this objective, the public health infrastructure will be expanded to include communities, businesses, educational groups, health care organizations and the media. In this effort, however, CDC will maintain its commitment to serve as a public health leader by continuing to effectively partner and enhance relationships with state and local health departments.

The reorganization will not affect DTBE resources because TB funding is a Congressional line item that is allocated to CDC for distribution to specific programs. Since CDC is prohibited from advocating for additional dollars for any particular program, external groups and stakeholders would need to convey needs to Congress. However, CDC acknowledges the need to internally educate new leaders and organizational components that will play a role in establishing future goals, such as the Office of Strategy and Innovation and the Office of Human Capital and Professional Development. For example, DTBE could inform these offices about TB elimination goals and emphasize the importance of this initiative. Communication will be particularly critical for CCID because none of the national elimination or eradication programs for TB and other infectious disease have adequate resources.

Instead of viewing the reorganization as a process to minimize TB funding, ACET should use the new structure to take advantage of new opportunities. For example, a case can be made for CDC to enhance both domestic and global partnerships to achieve TB elimination. CDC encouraged ACET to express additional concerns about the new structure through letters to Dr. Gerberding, e-mail communications on the CDC web site or other venues. This approach will ensure that as the organizational design is finalized, CDC is aware of ACET's priorities and interests.

Update on the TB Control Guidelines

Dr. Castro described progress to date in further development of the guidelines for preventing transmission of *Mycobacterium tuberculosis* (*M.tb*) in healthcare facilities. The guidelines contain 411 references and outline recommendations in the first 100 pages. This approach was taken to avoid citing other documents throughout the guidelines. Key points highlighted in the guidelines are as follows. The need for risk assessment is emphasized due to variations in TB risks by setting. This recommendation should guide the frequency of screening. The hierarchy of controls is reaffirmed in order of importance: administrative controls, environmental controls and personal protection.

The role of the first generation QFT test (QFT-1g) is discussed, but the guidelines will be updated after QFT-2g is licensed. The importance of bioterrorism and preparedness

for SARS and other infectious diseases is emphasized. Supplement 4 is devoted to respiratory protection and describes the performance, types and effectiveness of different devices. The guidelines recommend that training be conducted and fit testing be performed "initially and periodically thereafter." Frequency should be based on local decisions for risk assessment, maintenance and reuse rather than annual fit testing. To address the issue of personal respiratory protection against infectious agents in more detail, CDC will sponsor a stakeholder meeting in September or October 2004. The Occupational Safety and Health Administration (OSHA) will be one of the key stakeholders in attendance.

The time-line to finalize the guidelines has been revised as follows. The cross-clearance process by five CDC centers, institutes and offices will be completed on June 25, 2004. DTBE will incorporate revisions by July 9, 2004; obtain clearance from NCHSTP by July 16, 2004; and publish the *Federal Register* notice on August 1, 2004. The public comment period will close on October 1, 2004. DTBE will revise the document based on public comments by October 15, 2004; obtain approval from the second CDC clearance process on October 31, 2004; and submit the guidelines for publication in the *Morbidity and Mortality Weekly Report* (*MMWR*) in October or November 2004.

Dr. Michael Tapper is the ACET liaison for the Society for Healthcare Epidemiology of America. He described events that led to ACET's recommendation in 2001 to revise the 1994 TB control guidelines. High rates of nosocomial transmission were strongly emphasized in the 1994 document, but the focus on this issue will decrease in the 2004 guidelines. Transmission rates in healthcare settings are not nearly as high as previously reported. The 1994 document noted the critical importance of frequent tuberculin skin testing (TST), but healthcare workers (HCWs) were found to be vastly over-tested due to regulatory mandates or published recommendations in response to outbreaks. The 2004 guidelines will provide guidance on conducting risk analyses in the current environment of declining TB.

Fit testing of respirators is the most controversial section of the 2004 guidelines. OSHA established the TB standard with the following requirements. TST must be performed according to CDC guidelines and HCWs must be fit tested for any respirator. Fit testing of respirators must be conducted in accordance with OSHA mandates and recommendations established by the CDC National Institute for Occupational Safety and Health (NIOSH). Respirator programs should be developed to teach HCWs to properly don a respirator and ensure proper fit with an effective seal against a biological agent. Administrative programs should also be created to train, supervise and monitor appropriate use of respirators among HCWs.

N95 respirators and airborne isolation rooms are now recommended for exposure to presumed or known cases of smallpox, SARS and avian influenza. N95 respirators may also be used in other settings where chemical or airborne agents would require a higher level of protection. Several professional groups and unions pointed out that the TB standard was no longer appropriate due to the dramatic decline of TB rates throughout the United States. In response to petitions and lobbying efforts, OSHA officially withdrew the TB standard on December 31, 2002. Instead of reverting back to CDC's guidelines, however, OSHA announced that regulation of respirators in healthcare settings would be covered under the General Industry Respiratory Protection Standard (GIRPS).

GIRPS requires annual fit testing with a medical assessment to evaluate the HCW's physical ability to wear a respirator. The mandate also requires an administrative program to annually review the success of the institution's respiratory program. When responsibility for respirator certification was transferred to NIOSH in 1995, U.S. manufacturers were no longer required to certify respirators for both filtration and fit characteristics. As a result, respirators are not certified in terms of quality and proper fit for the average human face. Many professional groups and unions have pointed out that GIRPS will place an enormous administrative and economic burden on healthcare facilities. OSHA previously granted a six-month postponement before enforcing GIRPS, but is not expected to grant another extension. The mandate becomes effective on July 1, 2004.

Dr. Christopher Coffey of NIOSH is the author of several solid studies on fit characteristics of N95 filtering face piece respirators. He summarized key findings from these data. NIOSH has performed three rounds of testing since 1996. In the first study, a simulated workplace protection factor test was conducted on several N95 filtering face piece respirators. A panel of Los Alamos National Laboratory workers was selected to represent the population of face sizes in the United States, but NIOSH is now modifying this cohort. The results widely varied because some respirators adequately fit with an assigned protection factor (APF) of at least 10, while the APF of other respirators was fairly low.

A similar pattern was seen in the second study. Of 18 respirators, only three met the APF of 10 without fit testing and six did not meet the APF of 10 with fit testing. Based on the test results, NIOSH concluded as follows. The incremental benefit is less if a well-designed respirator passes a fit test than if a poorly-designed respirator passes. An APF of 10 is not unrealistic if a solid process is implemented to ensure that the respirator was designed with good fit characteristics. An APF of 5 could be achieved by many more respirators without the need for a major redesign. Fit testing methods have high error rates with some false-positive results of nearly 20%. This outcome may lead

to passing HCWs who should have failed the fit test. Overall, fit testing was found to be a necessity of a respirator program.

At this time, NIOSH is proposing to incorporate a total inward leakage test into the requirements to ensure that each NIOSH-certified respirator has a good fit. The new language will not require formal rule-making; instead, a clause in the existing requirements will be used stating that NIOSH has authority to conduct any additional testing it deems necessary to ensure respirators protect wearers. NIOSH plans to include the total inward leakage test into the requirements for N95 respirators in the next year. NIOSH is also exploring the possibility of completely eliminating fit testing for respirators with an APF of 10 out of the box and only requiring fit testing for respirators with an APF <10. NIOSH has not yet reached a decision on this issue.

ACET noted several reasons to delay OSHA's enforcement of GIRPS on July 1, 2004. The focus must now shift from fit testing to good fit characteristics because infectious diseases other than TB are contingent upon N95 respirators. With the current fit testing paradigm, the rate of passing HCWs who will not be protected is 51%-84% and the rate of passing HCWs who should have failed the fit test is 3%-11%. No evidence has been gathered to demonstrate that fit testing is applicable to healthcare settings. Healthcare facilities will spend a tremendous amount of time and resources complying with GIRPS. These efforts should be devoted to the more critical components of both the TB and emergency preparedness hierarchy of controls. CDC's draft 2004 TB infection control guidelines explore the possibility of eliminating annual TST in low-incidence facilities. GIRPS contradicts this guidance because the same institutions with low TB incidence would be required to perform annual fit testing of N95 respirators.

ACET considered whether any actions would be effective at this point since GIRPS becomes effective in eight days. OSHA plans to enforce the mandate on July 1, 2004 despite strong opposition from unions and healthcare facilities, guidance from CDC leadership and consultations with professional groups. Based on clarification from CDC about ACET's role in this process, a motion was properly made by a voting member to take the following actions.

ACET will write a letter to recommend that enforcement of GIRPS on July 1, 2004 be delayed and its applicability be reassessed. The letter will list four reasons to support ACET's recommendation: CDC's upcoming stakeholder meeting with OSHA; new data recently published in the scientific literature; the inconsistency of GIRPS with CDC's draft TB infection control guidelines; and no scientific evidence to demonstrate the necessity of GIRPS in protecting HCWs. The letter will be addressed to the Honorable Elaine Chao, the U.S. Department of Labor Secretary; copies will be distributed to the HHS Secretary and Mr. John Henshaw, the Assistant Secretary of Labor. **The motion was tabled** to allow ACET to refine the language.

Update on U.S.-Mexico Border Health Activities

U.S.-Mexico Border Health Commission (BHC). Ms. Eva Moya, an ACET liaison for BHC, described progress to date on Border health initiatives. The Binational TB Card Project provides quality case management services for patients who travel between the United States and Mexico. Since April 2003, >260 cards have been issued in pilot sites in four U.S.-Border states and >60 patients received follow-up care. Cards are now being issued in Chicago, Tennessee and Washington due to increased travel to non-Border states among TB patients. Results from the project to date confirm that adherence to treatment is much more successful when binational case management is implemented and patients are tracked. CDC will conduct a comprehensive evaluation of the project.

BHC received funding of $3 million in March 2004 to support and enhance TB elimination efforts and laboratory capacity in the Border region. BHC celebrated World TB Day in Tijuana in April 2004. The event was marked by major press coverage and extensive participation by all Border states, the Mexico government and U.S. federal agencies. Each TB card pilot site presented reports and appropriate authorities issued a TB proclamation. BHC is developing *Healthy Border Health Cards* to reinforce and promote key prevention and education messages in English and Spanish to communities. The user-friendly and pocket-size health cards are now being field tested with community health workers and consumers. Of the ten cards that will be created, one will focus on TB.

BHC used World Health Day in April 2004 to increase awareness of Border health issues. In partnership with CDC, BHC launched the first "Immunization Week in the Americas" with a focus on Border health in April 2004. The second and third Immunization Weeks will be held in July and October 2004, respectively. BHC's planning and coordinating efforts are underway to prepare for Border Binational Health Week in October 2004. The major event will be launched in partnership with the Mexico government, U.S. federal agencies, ten Border states and local communities. Binational steering, regional and central committees have been established for the planning process. The theme will be *Families in Action to Improve Health* and the primary topics will focus on access to care, immunization across the life span and healthy lifestyles. The planning committees have agreed that infectious diseases will be a major area of discussion during the event.

Ten Against TB (TATB). Dr. Miguel Escobedo, an ACET liaison for BHC, described other ongoing efforts to address TB in the Border region. TATB held a meeting during World TB Day to finalize the Border TB Strategic Action Plan with four critical focus areas: surveillance, case detection, case management and laboratory infrastructure. TATB is collaborating with BHC to eliminate barriers to binational transfer of specimens

and medications. The process for Mexico-to-United States transfers has been fairly successful to date, but an effective strategy for United States-to-Mexico transfers is still being developed.

TATB recommended that BHC strongly emphasize the need for confidentiality to the media. This concern resulted from a Spanish television station that publicly announced the name of a Mexican patient in California who was detained for violating a health authority by taking medication. TATB partnered with the Francis J. Curry Center to implement training events throughout the Border. These conferences included nearly 800 physicians, nurses and community workers from both the United States and Mexico. TATB assisted in planning the International Union Against Tuberculosis and Lung Diseases 2004 conference. The meeting focused on trans-Border TB control issues and was extensively represented by Border TB workers.

TATB recently held an event to celebrate 12 years of Project Juntos (Together). Under this initiative, >1,000 active TB cases in Mexico have been managed; a 55% cure rate has been achieved from management of >85 MDR-TB cases; follow-up care has been provided to >4,000 TB contacts; and >20,000 home visits have been made. The 55% cure rate was based on established protocols that were used to follow patients for ten years. No reactivation of TB was seen for at least two years.

Project Juntos also co-sponsors numerous training events; maintains long-standing relationships with the Migrant Clinicians Network (MCN) and Migrant Health Stream; and seeks guidance from an advisory committee represented by physicians and staff from Health Resources and Service Administration (HRSA) community health centers (CHCs). *Grupos Sin Frontera* and Los Dos Laredos are extensively collaborating with Rotary International and the American Red Cross to develop a Border TB strategic plan. The two organizations are also partnering with TBESC to better analyze and define MDR-TB in the Border region.

ACET and CDC commended the diligent efforts of BHC and TATB in developing activities to increase awareness of TB in the Border region. For example, BHC is now distributing binational TB cards in Chicago because the city has the second largest number of Mexicans in the United States. TATB's inclusion of surveillance as a key focus area in the Border TB strategic plan will strengthen capacity to measure the burden of disease and plan for services. The *Healthy Border Health Cards* initiative will compliment the binational TB card project and further improve cross-Border activities.

ACET and CDC also made suggestions for BHC and TATB to consider. Chicago is not located in a Border state, but efforts should be made to include the city in BHC activities. BHC and TATB should explore potential opportunities that may result from CDC's new organizational structure. For example, the integrated design may provide a

better approach to respond to Border health needs. BHC and TATB activities for binational infectious disease surveillance, immunization and TB would all be addressed by CCID.

BHC and TATB agreed that significant progress has been made in Border health initiatives, but several key challenges still exist. Although Chicago will be extensively involved in Border Binational Health Week activities due to its large Mexican population, BHC needs additional funding and technical support to expand the binational TB card project to other areas with a significant TB burden. Resources are also needed for training, dissemination of materials and assessment of the initiative. BHC continues to strongly advocate for case management and care to immigrants, migrants and undocumented persons, but U.S. public health agencies have not been involved in these efforts. BHC funding is primarily used to support prevention activities in the Border that are developed and implemented by regional committees and community-based groups. These dollars cannot be allocated to healthcare facilities for care and treatment of immigrants, migrants and undocumented persons.

Overview of Overseas TB Screening and Stateside Notification

Dr. Susan Maloney, of the CDC Division of Global Migration and Quarantine (DGMQ), described the background, current activities and future directions of this initiative. For the first time in 2002, the foreign-born proportion of TB cases exceeded the U.S.-born proportion and is now >50% of all TB cases in the United States. The gap in TB rates continues to widen based on 2002 data that showed the foreign-born TB rate was eight times higher than the U.S.-born rate. This issue was also emphasized in the Institute of Medicine (IOM) *Ending Neglect* report in 2000. "Maintaining TB control with a focus on foreign-born persons" was one of the five broad recommendations made to eliminate TB in the United States in the future. CDC recognizes that overseas screening and stateside notification are critical areas in preventing TB among foreign-born persons.

According to 2002 data, ~59 million migrants enter the United States each year. Of those, 30 million are short-term visitors without visas; ~28 million have non-immigrant visas; 411,266 are immigrants and refugees; and 275,000 are undocumented migrants. However, this estimate is probably low. The number of "status adjusters" in the United States is 679,305. This population includes migrants who have different types of visas or are undocumented and apply for a permanent resident visa while in the United States. Of ~59 million foreign-born persons who enter the United States each year, ~58 million are not screened. This group includes students, transit aliens, treaty traders, foreign government officials, and temporary visitors, workers and family members.

Of the remaining ~1 million foreign-born persons, immigrants and refugees ≥15 years of age are screened overseas with a chest x-ray and acid-fast bacillus (AFB) smear if indicated; status adjusters ≥2 years of age are screened in the United States with a TST and chest x-ray. Overseas screening is conducted at one of 657 panel physician sites throughout the world. The Department of State pays for services of panel physicians under a contract, while DGMQ oversees and monitors medical examinations required for immigrants and refugees. Upon entry into the United States, paperwork of foreign-born persons is collected by the Bureau of Customs and Border Protection (BCBP), formerly the Immigration and Naturalization Service (INS), at one of eight quarantine stations. The paperwork is then circulated to notify health departments of the arrival of immigrants and refugees who are TB suspects.

The overseas TB screening process is designed to restrict travel or U.S. entry of persons with infectious TB, identify TB suspects who require stateside follow-up and evaluation, and notify receiving jurisdictions of the arrival of these migrants. Screening results are used to categorize foreign-born persons as “Class A” for infectious TB, “Class B1" for non-infectious active TB or “Class B2" for inactive TB. If a chest x-ray indicates active TB, three AFB smears must be performed overseas. Class A migrants have positive AFB smears, cannot enter the United States and are advised to obtain treatment. An application can be submitted for a waiver if the migrant can demonstrate that the AFB smears are negative. Class B1 migrants can travel to the United States, but jurisdictions are notified upon arrival.

CDC’s 2003 data showed the following results. Of 7,649 immigrants and refugees entering the United States for whom DGMQ collected paperwork, 7,645 had Class B1 and B2 TB. Despite overseas screening, follow-up in the United States will detect active TB in 3%-14% of Class B1 migrants and up to 4% of Class B2 migrants. Follow-up in the United States detected positive AFB smears in 2% of B1 migrants and 1% of B2 migrants. For both B1 and B2 migrants, 30% are not evaluated with AFB smears upon U.S. entry and 20% have blank data. The time from the overseas examination to U.S. arrival is <3 months and the time from U.S. arrival to evaluation by local health departments is ~1 month. DGMQ is taking several actions to address these challenges.

First, DGMQ established the Quality Assessment Program (QAP) in 1999 to ensure the quality of the overseas screening examination. The standardized program uses specific tools to monitor 657 panel physician sites. A multi-disciplinary team of physicians and laboratorians recommends remediation or removal and also provides onsite training and consultation. DGMQ makes QAP visits based on the volume of migrants and disease prevalence rates of TB and HIV. From 1999-2004, QAP teams made 170 site visits in 34 countries. Post-intervention evaluation data demonstrated a 50%-55% improvement rate.

DGMQ is considering several options to expand QAP, such as recovering costs and user fees as well as engaging in multipartite collaborative efforts with other countries that receive a large amount of migrants. DGMQ will participate in a meeting with Canadian and Australian health officials to explore the possibility of sharing resources to oversee assessments. Fraud prevention is another major component of QAP. DGMQ applies stringent procedures to ensure panel physicians confirm the identity and passports of applicants and escort persons to and from x-ray areas. DGMQ has dismissed numerous sites due to fraud.

Second, DGMQ is making efforts to resolve limitations with the screening algorithm of the chest x-ray and AFB smear. A study was conducted in Vietnam in 1999 to determine the efficacy of overseas TB screening among >1,000 persons with active TB. Based on chest x-rays, 7% were smear-positive with Class A TB and 93% had Class B1 TB. After applying the gold standard of a TB culture, positive results were found in 77% of Class A smear-positive persons and 11% of Class B1 persons. The study found the efficacy of overseas TB screening to be 75% for infectious TB and 34% for active TB defined as culture-positive.

DGMQ is also engaged in several research efforts focusing on the screening algorithm. CB-18 is a new sputum specimen processing method that showed a 30% increase in AFB sensitivity and a 10% decrease in AFB specificity. CB-18 is now being evaluated with PCR to address this issue. QFT, TST and serologic antigens for active TB are being analyzed for potential inclusion in the overseas screening algorithm. Local TB culture capacity is being reviewed to determine the feasibility of introducing and monitoring directly observed therapy overseas. Research findings are being applied to revise technical instructions for the overseas TB screening algorithm, apply new diagnostic tests, address TB laboratory and treatment issues, and analyze the validity of the examination.

Third, DGMQ is developing an electronic disease notification system (EDNS) to improve stateside surveillance of TB notification and follow-up. Evaluation data show that up to 21% of migrants with B1 and B2 TB can be lost if BCBP fails to identify the stamped Public Health Service alert in the visa. An additional 20%-30% of migrants with B1 and B2 TB can be lost when quarantine stations mail notification forms to health departments.

EDNS software and infrastructure have been built; national standards have been developed for performance and data collection; pilot tests are being performed in eight health departments; and a pilot project will be implemented to transmit data from overseas sites to U.S. health departments. Efforts will be made to broadly implement EDNS in all 50 states in 2005 or 2006, but funding must first be secured and sustained. EDNS will improve the timeliness and completeness of sending notifications. Data and

reports will be downloaded to health departments through an automated process. Capacity will be enhanced to evaluate overseas screening and domestic follow-up.

DGMQ's other activities to improve TB control and prevention among foreign-born persons are as follows. DGMQ and TBESC are conducting a population-based study of TB among migrants to examine immigrant status and identify other foreign-born groups to screen. DGMQ is partnering with the Division of Immigration Health Services (DIHS) to provide screening and treatment to undocumented immigrants. DGMQ is engaging in initial discussions with the Bureau of Citizen and Immigration Services, formerly INS, to determine whether authority for the civil surgeon screening program can be transferred to CDC.

DGMQ provided additional details about the overseas TB screening and stateside notification process in response to ACET's questions. First, DGMQ expects to partner with Mexico in the future to conduct research on CB-18 or other diagnostic tools. The efficacy of TB screening in Mexico would be analyzed as part of these studies. Second, panel physicians are not charged application fees at this time. DGMQ's proposal to recover costs and user fees would not impinge on the business of panel physicians.

Third, DGMQ's entire budget for the panel physician program is devoted to travel costs for ~32 overseas visits each year. DGMQ is currently conducting cost-effectiveness and cost-benefit analyses to compare resource needs for two options: expanding the program versus providing additional resources to ports of entry. DGMQ recently received bioterrorism dollars to expand the program to include 25 additional quarantine stations at ports of entry in the United States. Fourth, DGMQ will extensively engage hospitals and HRSA CHCs in future phases of EDNS since migrants and refugees with active TB or LTBI frequently present to these facilities for care.

Overview of TB Vaccine Research

Dr. Michael Kurilla is the ACET *ex officio* member for the National Institutes of Health (NIH) National Institute of Allergy and Infectious Diseases (NIAID). He summarized the NIH/ NIAID TB program and research initiatives. NIH's mission is to support and conduct research to strengthen the foundation of scientific knowledge for new healthcare interventions. Of NIH's 27 institutes and centers, NIAID has the lead for TB research and encourages the submission of applications. Of NIH's total TB research budget of ~$120 million in FY'03, NIAID allocated ~$85 million to TB pathogenesis and the development of TB drugs, vaccine and diagnostics.

NIAID has control over TB research it funds through contracts, but has no authority over applications that are unsolicited, peer reviewed, scored by external panels and funded

on the basis of merit. For TB research through contracts, NIAID allocates $4.4 million to TB drug development, $1.7 million to TB vaccine development, $508,362 to TB diagnostics development, and ~$31 million to TB pathogenesis. For generic therapeutic discovery or development, NIAID's established paradigm is followed in a step-wise process: identification of fundamental science; identification of a drug, vaccine or other target; validation and screening of the target; efficacy studies with animals; preclinical studies through the FDA regulatory process; and clinical studies and trials with humans to obtain regulatory approval.

Researchers must answer three key global questions in a generic therapeutic program. First, does the underlying science support the proposed activities? Second, are adequate funding mechanisms available to perform required activities? Third, does an infrastructure exist to conduct necessary studies? NIAID has made significant efforts to expand and improve its TB program portfolio over the past 15 years. Fundamental science projects are now focusing on microbiology, genomics, post-genomics, MDR-TB strains, and high-virulence versus low-virulence transmission. Projects to identify, validate and screen targets as well as efficacy studies are now focusing on diverse molecular tools and refinement of animal models for TB infection and disease. Preclinical and clinical studies or trials are now focusing on the human response to TB and adult and pediatric responses to BCG vaccination.

Since preclinical and clinical studies or trials are the most expensive components of the paradigm, NIAID created several research mechanisms to support these initiatives. These tools include grants and cooperative agreements for research, single and multiple projects and small businesses; domestic and international program announcements; grants to specifically address TB therapeutics research and TB as an AIDS-related opportunistic infection; and biodefense projects targeting MDR-TB. NIAID established a variety of training programs to ensure that both domestic and international TB researchers can successfully perform grant and cooperative agreement activities.
NIAID provides researchers with critical guidance during the training programs. For example, the desired clinical indication of a new TB vaccine and the vaccine format will influence the design of a clinical trial. A new vaccine could serve as a BCG replacement, BCG booster or therapeutic vaccination. PPD-negative adults, PPD-positive adults and HIV-positive persons could be addressed as well. The researcher must also decide whether the format should be a subunit, attenuated *M.tb*, recombinant BCG or DNA-based vaccine. NIAID contracts for new TB vaccines are highlighted below.

Under a TB research materials and vaccine testing contract, researchers can send candidate vaccines to Colorado State University for testing to determine if the minimum requirements are met for preclinical studies. To date, >120 candidate vaccines have been analyzed under the contract. Under a contract to characterize essential and non-

essential TB genes with animal models, multiple animal models with the same genetic materials are being tested for the first time. Data will be collected to demonstrate the relevance of various animal models on human disease. Under the "Millennium Vaccine Initiative," domestic and international experts are engaging in a tremendous collaborative effort to identify novel TB vaccines. The program has been successful in optimizing a recombinant and multi-component subunit vaccine.

The *M.tb*72F vaccine was administered to humans in Phase I trials earlier in the year. The vaccine includes *M.tb*39 and *M.tb*32 antigens and was identified by testing healthy PPD-positive donors for immune responses to LTBI. The two genes were spliced with an innovative technique and mixed with the AS02A adjuvant. The Phase I trials represent the first time a new TB vaccine has been tested in humans in over 60 years. NIH grant funds were used to develop and test a recombinant BCG30 vaccine with animal models. The vaccine appears to be superior to BCG and has undergone the FDA regulatory clearance process. Phase I trials will be initiated later in the year. NIAID's Vaccine and Treatment Evaluation Units (VTEUs) were established in 1962 at multiple sites throughout the country and have resulted in >110 Phase I, II and III clinical trials for all vaccines since 1995. The VTEUs will be used to conduct Phase I TB trials in the United States, but Phase II trials will most likely not be initiated in the United States due to insufficient patient populations.

NIAID is responsible for nearly all contributions to TB vaccine development, but efforts are being made to identify partners to advance vaccine candidates to preclinical studies and Phase I clinical trials. NIAID also needs partners for vaccine formulation, lot production and development of a clinical plan to proceed through Phase I, II and III trials. Despite these barriers, NIAID has placed strong emphasis on new therapeutics for TB/HIV co-infection over the past few years. The existing paradigm was modified for this effort because many HIV opportunistic infections are not suitable for pharmaceutical companies to develop therapies. Researchers can submit compounds with potential activity against TB to the TB Antimicrobial Acquisition and Coordinating Facility for screening. To date, researchers throughout the world have submitted 8,000-10,000 compounds for testing, including derivatives of existing compounds and new natural products. After *in vitro* testing, compounds are incorporated into animal models. The current candidates include 34 GKO or standard mouse models; 141 compounds approved for *in vivo* testing, excluding analogs of known TB drugs; and 41 compounds under consideration.

NIAID acknowledges that major issues and concerns must be addressed in TB/HIV co-infection treatment, particularly appropriate treatment for both infections; effective protection against infection or re-infection of HIV-positive persons; and the immune reconstitution reaction in TB/HIV co-infection. Several studies are underway to address issues related to TB/HIV co-infection, including CDC's TBTC Study 22 and international

research in Malawi, Peru, South Africa and Uganda. Although NIAID regularly communicates with CDC about ongoing TB research initiatives, caution must be taken in conducting joint studies. Funding for TB research is a Congressional line item that cannot be transferred between federal agencies.

For clinical trials with human studies, NIAID has an international contract under the TB Research Unit to analyze a wide array of TB-related studies and address complex biological TB issues, such as the human response to *M.tb*, disease transmission, surrogate markers of infection and disease, and protective immune response. A community study in Uganda is aiming to answer several research questions on human protective immunity to *M.tb*. International sites for clinical studies and Phase I and II trials are located in Africa, Brazil and the Philippines.

NIAID has a public/private partnership with the Global Alliance for TB Drug Development (Alliance) to conduct preclinical studies and clinical trials. NIAID was one of the founding stakeholders that established the Alliance in 2000. The Alliance identifies potential compounds that can be advanced to preclinical development and then initiates the FDA regulatory approval process to obtain investigational new drug (IND) status. NIAID is also making progress in the advanced drug development arena. Recent animal data suggest that TB treatment can be shortened by two months when INH is replaced with moxifloxacin. This outcome was found to be extremely encouraging.

Other advanced drugs currently under development include PA-824, oxazolidinone and thiolactomycin. A review of PA-824 efficacy showed that the drug is as potent as INH, bactericidal against replicating TB, active against most MDR-TB strains and orally bioavailable with formulation. Other analogs demonstrated greater *in vitro* activity than PA-824, but less *in vivo* activity. NIAID and the Alliance are now advancing the drug through the preclinical development phase and expect to submit the IND application to FDA later in the year.

Overall, NIAID's role in research of TB and other mycobacterial diseases is as follows. NIAID primarily allocates funds through basic research and target identification grants. NIAID is using a large structural genomics consortium of 70 laboratories to support crystallography studies of TB genes as potential drug targets. NIAID serves as a broker by linking small research companies to grantees that have an established infrastructure and more resources. NIAID supplements its grant portfolio with targeted contracts to fill gaps in the genetic therapeutic discovery and development paradigm as well as to meet the needs of other requirements. NIAID anticipates that data from its current TB research grants, contracts and cooperative agreements will be publicized over the next several years.

CDC agreed that caution must be taken in jointly conducting TB research projects with NIAID due to restrictions on interagency transfer of funds. However, opportunities are still available for the two agencies to achieve greater synergy. For example, NIAID can attend CDC's biannual TB clinical trial meetings to identify potential research populations in the United States and international countries. NIAID can also participate in quarterly conference calls or face-to-face meetings convened by the Federal TB Task Force to develop a plan in response to the IOM recommendations.

ACET returned to the tabled motion and reviewed the draft language. ACET recommended that a letter be sent to the U.S. Department of Labor Secretary in OSHA. The letter should request a delay in enforcing GIRPS on July 1, 2004, ask for a reassessment of GIRPS's applicability, and list four reasons to support the request. ACET made several suggestions to refine the draft language; **the motion was unanimously approved** with no further discussion. The entire motion as finalized and approved by ACET is appended to the minutes as Attachment 1.

Update on QFT

Dr. Jerry Mazurek of DTBE explained that QFT is an *in vitro* whole-blood assay for *M.tb* infection. The test measures interferon-γ release from lymphocytes after incubation with *M.tb* antigens and does not differentiate between active TB and LTBI. Efforts are underway to improve and advance specific antigens and test methods. Three generations of QFT are currently being considered for commercial use or availability. QFT-1g is an FDA-approved test that uses PPD, control antigens and a less sensitive ELISA assay than other versions of QFT. QFT-2g is available outside the United States, but is now being reviewed by FDA for licensure approval. The test uses ESAT-6 and CFP-10 antigens to test responsiveness to TB and an ELISA assay that is 30 times more sensitive than QFT-1g. The third generation QFT test (QFT-3g) is under development and includes ESAT-6, CFP-10 and TB 7.7 antigens. This test is easier to use in remote locations.

QFT-2g is considered to be an improvement over QFT-1g due to its specificity with ESAT-6 and CFP-10 antigens. These antigens have been demonstrated in all *M.tb* strains tested to date, but have not been found in commercially available BCG vaccine sub-strains. ESAT-6 and CFP-10 antigens have only been detected in three of the 18 most commonly recovered non-tuberculous mycobacteria. QFT-2g is performed by drawing blood into a heparin tube; making 1 ml aliquots of the blood; adding three drops of saline, ESAT-6, CFP-10 and a control substance to four different wells; mixing and placing the blood in an incubator for overnight storage; harvesting plasma from above settled cells; and using a "sandwich" ELISA to measure the amount of interferon-γ produced compared to standard controls. The data are then input into a computer for

an interpretation of results. This method will be modified in QFT-3g due to the ability to place ESAT-6 and CFP-10 antigens in one tube.

CDC is continuing to collect and analyze data supporting the use of QFT-2g from sensitivity studies among culture-confirmed TB suspects and specificity studies among BCG-vaccinated Japanese students, U.S. Navy recruits and other persons with no known risk of exposure. In the Japanese study, subjects were enrolled from July-October 2002 at four hospitals and four colleges in Japan. Of 152 untreated adult TB suspects, 119 had culture-confirmed TB, 18 had usable QFT-2g results and one had indeterminate QFT-2g results. A cohort of 216 BCG-vaccinated student nurses with no known TB exposure was enrolled as well. QFT-2g sensitivity was 89% using a change in interferon-γ of ≥0.35 IU/mL to either ESAT or CFP-10 antigens. Of 118 subjects with culture-confirmed TB, 105 responded to either ESAT-6 or CFP-10. QFT-2g specificity was 98.1% using the same cut point. Of 216 unexposed nursing students, 212 did not respond to either ESAT-6 or CFP-10. These results demonstrate that QFT-2g sensitivity and specificity are comparable to or better than QFT-1g or TST as used in Japan.

In a QFT-2g study among 900 Navy recruits enrolled in January 2004, 841 had initial QFT-2g and TST results. Of seven recruits with positive QFT-2g results, the specificity was 98.8%. Of 24 recruits with positive TST responses ≥15 and 44 recruits with positive TST responses ≥10, the specificity was 97.1% and 94.8%, respectively. This finding demonstrates that if a higher TST cut point of ≥15 is used, the number of persons found to be positive with QFT-2g will be dramatically different. In an Australian study with 41 culture-confirmed TB suspects, 33 had positive QFT-2g results. Of 100 subjects in the study with no known risk of TB exposure, 95 had negative QFT-2g results. In a study in a Ho Chi Ming City hospital among 1,107 visa applicants with QFT-2g and TST results, 35 had positive cultures. QFT-2g sensitivity was >70% among 35 subjects with culture-confirmed TB based on a preliminary data analysis, but the possibility of prior treatment cannot be excluded. In other studies with similar assays and ELISpot studies among TB contacts, QFT-2g showed a greater association with exposure.

DTBE held a consultation on June 11-12, 2004 to review recent data on QFT-2g; key outcomes from the meeting are as follows. QFT-2g specificity is adequately documented and sensitivity appears to be similar to TST. After FDA approves QFT-2g, CDC will need to develop guidelines and studies in children and HIV-infected persons will need to be conducted. The meeting participants acknowledged that CDC guidelines will influence evaluation and implementation of QFT-2g. Support for new diagnostics must be balanced with appropriate cautions in implementation. Resource limitations associated with the use of QFT-2g must be recognized.

ACET extensively discussed preliminary data from the studies. QFT-2g specificity is dramatically better than QFT-1g, but concerns with sensitivity must be addressed if CDC's goal is to use QFT-2g to evaluate persons for LTBI. Caution must be taken in applying culture-positive results from international studies because quality control methodologies in laboratories may not be as solid as those in the United States. ACET was pleased that during the recent DTBE consultation, the development of QFT-2g guidelines was discussed and resource barriers programs will encounter in implementing the test were noted. ACET asked CDC to consider two key issues while developing the guidelines. Programs should be encouraged to use QFT-2g as a second test to confirm or validate TST results if CDC continues to recommend TST. Different settings where QFT-2g will potentially be used should be described. For example, some ACET members are now using QFT-1g in HCWs, foreign-born persons and inmates and expect to also use QFT-2g for these populations after the test is approved.

CDC and FDA share ACET's concerns about QFT-2g sensitivity, particularly in children, immunocompromised persons and other vulnerable populations. CDC and FDA are now evaluating the impact of treatment on improving QFT-2g results. However, CDC believes that better cohorts can be used to provide more definitive and rapid answers on QFT-2g sensitivity. For example, TBTC studies could be conducted in the United States with an HIV-infected population or among persons with an early TB diagnosis. Efforts should now be made to readily identify and endorse high-priority studies in various populations, develop appropriate protocols and obtain approval from an Institutional Review Board. This approach will ensure immediate implementation of the studies when resources become available.

CDC acknowledges the need to balance continued development of a new technology with great promise and the responsibility to provide the best possible care to patients and avoid placing persons at risk. Overall, CDC's position is that both QFT-2g and QFT-3g can be used to improve TST. CDC must make positive recommendations in order for further development of QFT-2g to continue. In the near future, DTBE will circulate drafts of the QFT-2g guidelines and other issues related to the test. ACET's advice and comments on the documents will be solicited.

Update on TBTC

Dr. Elsa Villarino of DTBE described TBTC's ongoing activities, future agenda and budget constraints. TBTC now has 28 clinical sites worldwide with links to local TB control programs. International sites that were recently added represent countries with high TB burdens. TBTC operates under formal bylaws and policies to fulfill its mission to conduct programmatically relevant research on the diagnosis, clinical management

and prevention of TB infection and disease. TBTC's experienced sites and investigators are conducting activities with a state-of-the-art scientific agenda and a solid administrative structure that includes internal quality assurance mechanisms, protocol development techniques and a regulatory process. TBTC now has a core science group that comprehensively reviews important questions related to TB therapeutics; identifies studies being conducted or planned by other research groups; and obtains input from TBTC members, DTBE, ACET and NTCA to prioritize critical issues. DTBE began funding TBTC in 1998 and maintains its coordinating center and data.

Several TBTC studies are underway to improve treatment of TB infection and disease. These efforts are focusing on more effective, safer and better tolerated therapies that will result in a shorter treatment duration of <6 months or <9 months for LTBI; less frequent dosing; better outcomes for patients at high risk for treatment failure or relapse; and improved identification of patients with LTBI and risk of progression to active disease. Enrollment has been completed for three TBTC studies since 1995; key outcomes from the five ongoing studies are highlighted below.

Study 26 is aiming to enroll 8,000 high-risk patients with LTBI; 3,086 patients have been enrolled since June 2001. The original five-year enrollment cycle will most likely need to be extended to June 2007 to reach the target of 8,000 subjects. The Study 26 cohort will receive 270 daily doses of INH for nine months or 12 doses of once-weekly INH/RPT therapy for three months. Study 26 sub-studies are focusing on the impact of chronic viral hepatitis in tolerating LTBI therapy; the pharmacokinetics (PK) of rifapentine in children <11 years of age; the potential correlation between hypersensitivity syndrome and influenza-like illness caused by Study 26 drugs; and the potential presence of serum antibodies resulting from Study 26 drugs.

Study 27 is a Phase II randomized clinical trial for active TB disease that was created with a factorial design to analyze the role of moxifloxacin in a TB drug regimen. The objective of the study is to compare the culture conversion rate of patients treated with a regimen of INH, rifampin (RIF), pyrazinamide (PZA) and ethambutol versus those treated with a regimen of INH, RIF, PZA and moxifloxacin. All patients in the study will be followed with a continuation phase regimen approved by ATS and CDC. Of 300 patients needed for Study 27, 155 have been enrolled to date. The Case Western Reserve University/Uganda site is responsible for 78 of the 155 enrolled subjects. CDC expects to complete enrollment by November 2004.

Available data applied to Study 27 include moxifloxacin's activity, comparability to INH and other drugs, and performance in mouse models, animal experiments and human studies on PK and toxicity. These data showed that of all available fluoroquinolones, moxifloxacin has the greatest potential for successful inclusion in an experimental TB

study. The results also demonstrated the potential for developing a regimen of shorter duration and administering the therapy intermittently in combination with other drugs. A PK evaluation is also being conducted under Study 27 to determine whether moxifloxacin PK is different in TB patients and if RIF therapy decreases the concentration of moxifloxacin. Healthy volunteers receiving moxifloxacin and RIF will be compared to Study 27 subjects receiving the INH/RIF/PZA regimen.

Study 28 has been proposed as a Phase II clinical trial to compare the microbiological activity and safety of a regimen with moxifloxacin versus the standard control regimen of INH, RIF, PZA and ethambutol. Results from two repeat animal studies showed much higher efficacy in the moxifloxacin regimen than the INH regimen. Study 28 will be designed to measure sputum-culture conversion. The findings will be applied to a Phase III clinical trial to determine the role of moxifloxacin in treatment regimens that are less than the standard six-month regimen.

TBTC drafted a proposal to address key issues related to the treatment of HIV-related TB, including the timing of anti-retroviral (ARV) drugs during TB therapy, interaction among TB and HIV drugs, and paradoxical reactions. TBTC members are currently reviewing the proposal, but funds are needed to further develop this project. TBTC is also interested in pediatric TB treatment issues, particularly the ability to treat childhood TB with once-weekly therapy and the necessity of prolonged therapy for disseminated and miliary TB.

With appropriate funding and staffing, TBTC capacity would be sufficient to concurrently implement the following activities from 2004-2007. On an annual basis, 300-480 patients could be enrolled in active TB studies; 150-300 patients in Phase II studies; 200-400 patients in special population studies; 1,000-1,500 patients in Phase III studies; 15-100 patients in PK studies; and 1,560 patients in LTBI studies. However, TBTC will have no capacity for LTBI studies until 2006 or 2007.

TBTC took several actions to reduce its FY'04 budget by $480,727 in response to DTBE's deficit. Contract payments were decreased, one site was permanently closed, ten sites voluntarily agreed to take reductions, plans to strengthen data management capacity were deferred, and funding was rescinded from the TBTC memorandum of understanding with the Department of Veterans Affairs (VA) and WESTAT. DTBE's projected deficit for FY'05 will impact the TBTC budget for the remainder of the 2005-2008 funding cycle. TBTC expected to receive $\leq$$9.2 million per year for each of the four years, but no cost of living increases will be possible unless new funds are identified. TBTC investigators are actively seeking non-DTBE funding sources to supplement current studies. The TBTC Executive Affairs Group and VA senior staff will jointly make decisions about budget adjustments.

ACET found TBTC's deficit to be particularly disheartening in light of budgets for NIH HIV/AIDS treatment groups. The least amount of funding for one group to conduct clinical research is $30 million per year and the cumulative budget of all groups will be $500-$700 million in the upcoming budget cycle. ACET acknowledged that AIDS is a devastating disease, but TB also results in severe adverse outcomes throughout the world. TBTC is the only group with existing capacity and infrastructure to perform TB clinical trials and address the burden of TB infection and disease. For example, TBTC's extremely valuable contributions to TB control include groundbreaking research on LTBI treatment and innovative studies on moxifloxacin. Several changes in the ATS/CDC/Infectious Disease Society of America treatment statement were directly related to TBTC activities and data.

Without additional funding, TBTC will be unable to conduct QFT studies and implement other projects in the future that will have a meaningful impact on TB treatment both domestically and internationally. CDC emphasized that despite the need to reduce expenditures, the TBTC infrastructure will be maintained. To support this effort, CDC and the Alliance are exploring and discussing potential mechanisms that can be used to leverage additional resources. Identification of an effective regimen that can cure TB in four months is one of the Alliance's stated goals.

TB and Tumor-Necrosis Factor Blockers

Dr. John Jereb explained that tumor necrosis factor-α (TNFα) agents are for patients with moderate to severe rheumatoid arthritis who do not adequately respond to or tolerate methotrexate or at least two other disease-modifying agents. Patients who receive TNFα blockers are sicker, have more advanced disease, and are problematic for TB control because the treatment and severe disease will decrease TST or QFT sensitivity in diagnosing LTBI. TNFα blockers perform with immune modulation or deficiency, but immune deficiency causes susceptibility to TB and other granulomatous infectious diseases. As a result, the agents are believed to result in the progression of LTBI to active TB disease. FDA has approved three TNFα blockers, but several new agents under development are expected to be approved in the future. The three approved TNFα blockers are described below.

Etanercept was the first TNFα blocker approved by FDA in the United States in 1998. The agent is a dimeric fusion protein of human nature and a soluble version of the TNFα receptor that would normally reside in cells. Etanercept binds free TNFα and lymphotoxin-α and causes minor lysis of macrophages and monocytes. The agent is approved for the treatment of rheumatoid arthritis, polyarticular-course junior rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis.

Infliximab combines human-murine monoclonal antibody, is highly specific for TNFα and binds to membrane-bound TNFα. Lysis of macrophages and monocytes is a side effect of infliximab that could lead to monocytopenia and contribute to progression of TB. The agent is recommended for administration with methotrexate because the murine component of the antibody is more likely to cause an immune response that negates the effects of treatment. Infliximab is approved for the treatment of rheumatoid arthritis, Crohns disease, ankylosing spondylitis, psoriasis and psoriatic arthritis. Adalimumab was approved by FDA in 2003 and is a recombinant human IgG1 monoclonal antibody with an activity profile that is similar to infliximab. This agent can also lead to monocytopenia and is only approved for the treatment of rheumatoid arthritis. In pediatric populations, the three TNFα blockers are only approved to treat junior rheumatoid arthritis.

Data gathered to date do not demonstrate significant differences in the roles of the three TNFα blockers in TB. TB was immediately detected in Phase III studies of infliximab. The data estimated that the rate ratio of this agent for TB would be four times greater if treated populations were comparable. The median onset of TB was ~12 weeks with infliximab. TB was not detected in treatment trials of etanercept. Preliminary data estimated that the TB incidence would be similar to the TB background rate with comparable populations. The median onset of TB was ~11 months with etanercept. Minimal data have been produced for adalimumab, but initial results suggest that the rate of TB will be similar to or a little less than infliximab.

Among patients receiving TNFα blockers, 50% have extrapulmonary disease and 50% of this subgroup have disseminated TB. Diagnosing patients with pulmonary involvement is extremely difficult because radiographic findings are non-specific. Moreover, patients with underlying chronic diseases may produce symptoms similar to TB and have increased mortality. Guidance to practitioners on TNFα blockers includes package inserts and letters from drug manufacturers, FDA advisories, and peer-reviewed publications with general suggestions to care for patients and prevent TB. The infliximab and adalimumab package inserts have a large boxed warning at the beginning of the text to inform providers that screening and prophylaxis are recommended for all patients. The etanercept package insert contains a bold warning in the body of the text to inform providers that a risk of TB exists and efforts should be taken to detect and prevent TB infection. FDA advisories refer providers to package inserts to reinforce these cautionary messages, but guidance is not given on specific actions to take.

To date, ~6 solid peer-reviewed papers have been produced on TB and TNFα blockers. A 2003 article published in *The Lancet Infectious Diseases* focused on mechanisms of action and clinical management of TNFα agents in TB risk. CDC's guidelines will be similar to the *Lancet* paper, but TB prevention and disease in the context of early

detection, diagnosis and treatment of LTBI and underlying conditions will be emphasized. CDC recognizes that adherence to the guidelines among general and family practitioners will be a challenge. Providers will need to screen for TB; treat LTBI in conjunction with TNFα blockers; and treat TB without direct clinical evidence to demonstrate the disease will be the same for TNFα blocker patients. However, CDC is optimistic that rheumatologists will modify practices due to strong leadership from the American College of Rheumatology (ACR).

CDC has taken several actions to further address TB and TNFα blockers. Collaborative efforts have been initiated with internal and external partners, including the California State TB Control Branch, ACR and FDA. Expert opinion guidance will be disseminated through an *MMWR* article that is currently being reviewed. The article summarizes California surveillance data on 12 TB cases associated with TNFα blockers from January 2002-September 2003. Of the 12 cases, 11 were taking infliximab, 11 had risk factors for LTBI and nine were taking immunosuppressive agents other than TNFα blockers.

The *MMWR* article will contain the following recommendations. The earliest possible preventive measures should be practiced to diagnose and treat LTBI. Screening for LTBI should be based on a history of TB risk factors because TST may be less sensitive. A TST cutoff of $\geq$5 mm should be used according to expert opinion and published case series. Providers should maintain a high index of suspicion of TB for patients being treated with TNFα blockers. In the future, CDC will convene a multi-disciplinary summit meeting with experts from ACR and FDA, but is now requesting ACET's advice on its current approach and future directions to address TB and TNFα blockers.

ACET supported CDC's current approach of advising practitioners to take the earliest possible preventive measures in diagnosing and treating LTBI and maintain a high index of suspicion for TB risk factors. However, concerns were expressed about the lack of solid data to support a TST cutoff of $\geq$5 mm in TNFα blocker patients. As a result, CDC's guidelines should strongly emphasize the need to closely monitor patients with previous LTBI or TB treatment to detect recurrence or reactivation of disease.

ACET agreed that the CDC/ACR collaboration will be effective in warning rheumatologists to screen TNFα blocker patients for TB. However, ACET advised CDC to immediately convene expert panels to develop extremely explicit recommendations. Because most rheumatologists are unfamiliar with TB, the guidelines should specifically outline the appropriate time to administer TNFα blockers versus LTBI treatment, proper situations to use a TST cutoff of $\geq$5 mm, and correct usage of QFT. CDC should also incorporate guidance into patient educational materials because this approach may prompt TNFα blocker patients to remind providers to screen for TB. ACET suggested

other important target audiences for CDC to consider while disseminating the TNFα blocker guidelines, such as health departments and gastroenterologists.

With no further discussion or business brought before ACET, Dr. Kawamura recessed the meeting at 4:46 p.m. on June 23, 2004.

ACET Business

Dr. Kawamura reconvened the meeting at 8:42 a.m. on June 24, 2004 and announced that she wrote a letter to the U.S. Department of Labor Secretary in OSHA in response to ACET's unanimously approved motion on the previous day. The letter would be sent later in the day; copies were distributed to ACET for review.

Dr. Kawamura entertained a motion to accept the previous meeting minutes; the motion was properly made and seconded by voting members. The February 4-5, 2004 ACET Meeting Minutes were unanimously approved with no changes or further discussion.

ACET proposed the following topics to be added to the ongoing list of agenda items.

- Presentation by OTPER on the role of bioterrorism dollars in strengthening the public health infrastructure and use of bioterrorism dollars for laboratory support since MDR-TB is a Class C agent. **[HIGH PRIORITY]**
- Presentation by HRSA on TB prevention and control in CHCs.
- Update on TBESC.
- Discussion of TB priorities in preparation of a potential change in HHS and CDC leadership.
- Update on international TB activities by the Alliance and the CDC Global AIDS Program (GAP).
- Overview of CDC's surveillance data systems.

TB Funding Allocations

Dr. Castro announced that DTBE's FY'05 deficit is anticipated to be $5.5 million based on the President's request and DTBE's projected needs and commitments. To balance the deficit, funding from targeted testing and treatment of LTBI projects, regional Training and Medical Consultation Centers (TMCCs), TBTC, TBESC and unobligated funds will be reduced by $5.5 million. The FY'05 TB cooperative agreement budget of ~$105 million will be allocated as follows: $89.2 million for core prevention and control activities, $6 million for regional TMCCs, $2 million for training and education of state

and local health departments, and $7.9 million for laboratory support. Under the $89.2 million budget for core prevention and control activities, $83.7 million will be for financial assistance and $5.5 million will be for direct assistance to state and local health departments.

Core cooperative agreement funds will be redistributed to match the changing epidemiology of TB and different patient profiles. Under the proposed plan, 80% of base funding will be retained and 20% will be redistributed. Criteria for the redistribution were developed based on a five-year average of areas with 40% of TB incident cases, 15% of U.S.-born minorities, 15% of foreign-born persons, 10% of Class A, BI and B2 TB, 5% of HIV co-infection, 5% of MDR-TB, 5% of substance abuse, and 5% of homeless populations. Based on this formula, 21 of the FY'05 grantees will sustain reductions, 31 will receive increases, and 16 that receive ≤$200,000 will not be affected.

From a geographical perspective, the redistribution will shift funding from northeastern to southeastern and western parts of the country. The only cooperative agreement funding that will be affected by the redistribution is $83.7 for financial assistance to state and local health departments. The laboratory support funding of $7.9 million will be redistributed with a different formula based on laboratory burdens of states. DTBE is making every effort to finalize and immediately circulate the redistribution plan to grantees since changes in funding will impact local decision-making.

ACET received a written public comment from Dr. Isaac Weisfuse, the Deputy Commissioner for Disease Control in the New York City Department of Health and Mental Hygiene. Dr. Weisfuse noted that DTBE's reallocation of FY'05 funds will result in a 21% decrease in the program's federal TB control dollars; an 11% reduction in the overall program budget; and a loss of jobs for 40-50 public health workers. Overall, the redistribution will lead to a tremendous decrease of ~$3.5 million. Dr. Weisfuse also expressed concern about the elimination of targeted testing funds. The letter was submitted into the public record by the Executive Secretary and is appended to the minutes in its entirety as Attachment 2.

ACET commended CDC for extensively soliciting input from NTCA, states and large cities to develop sound, fair and equitable criteria for the redistribution plan. However, ACET was extremely concerned about DTBE's considerable deficit of $5.5 million. At the federal level, CDC has announced that the *Healthy People 2010* (*HP2010*) objective for TB will not be achieved and is now proposing to establish a new national goal. At local and state levels, reduced funding to programs that have made significant progress in decreasing TB cases will ultimately lead to a resurgence of disease in these areas in the future. Targeted testing dollars have been completely eliminated in New York City and San Francisco. These programs achieved local TB control goals, but now have no

funding to advance to TB elimination strategies. Solid TB programs in Alabama, Baltimore and Mississippi will face severe adverse outcomes as well.

ACET shifted the discussion to creative and innovative strategies that can be implemented to advance the TB elimination effort and more effectively address populations in need of LTBI screening and treatment. Several suggestions were made for ACET, CDC and HRSA to consider.

ACET

- Replicate the HIV/AIDS approach for TB in which aggressive actions were taken and demands were made for additional funding. Encourage outside organizations representing communities, refugees, inmates, substance abusers, homeless populations and other affected groups to bombard the HHS Secretary with letters about the inadequate TB budget. Partner with community-based groups, grassroots organizations and other groups with strong networks to strategically and regularly launch TB outreach campaigns. "Put a face on TB" by displaying infants and children with TB on posters throughout the country. Establish TB booths at health fairs and other events.
- Emphasize the importance of TB to providers and constantly reinforce these messages. Incorporate TB into medical and nursing school curricula and include TB questions on board examinations. Encourage the Centers for Medicare and Medicaid Services to add TB as an indicator in the Health Plan Employer Data and Information Set. Establish relationships with the American Medical Association and other professional societies that represent internists, family practitioners, pediatricians and other private providers. Make TB presentations at national meetings of these organizations.

CDC

- Extensively communicate with and disseminate solid data to OTPER to demonstrate that TB is a bioterrorism agent due to its person-to-person transmission. Explore the possibility of creating an external bioterrorism advisory committee to provide guidance to OTPER. Ensure that ACET, DTBE and the Council of State and Territorial Epidemiologists are represented.
- Convene two events: a follow-up consultation with the Southeast African American participants and a meeting with private providers.
- Invite the National Health Plan Association and Rotary International to attend future ACET meetings.

HRSA

- Develop and enforce TB screening policies for CHCs because populations at risk for TB present to these facilities for care. Define TB as an essential component of primary care that should not require additional CHC resources. Develop and monitor indicators for TB screening and follow-up and require CHCs to adhere to these guidelines. Add TB to the health disparities list.

The federal agencies made comments in response to ACET's suggestions. CDC clarified that ACET would be within its purview to make a formal statement to the HHS Secretary and CDC Director about the lack of support for the TB elimination effort, the current TB environment in the United States, and DTBE's current and projected budget deficits. The letter could emphasize the impact these challenges will have on capacity to achieve TB elimination. The IOM report and the National Coalition for the Elimination of Tuberculosis (NCET) federal funding gap report could be referenced as well. Another action ACET could take is to further justify the need to apply bioterrorism dollars to TB by describing a model during the OTPER presentation and discussion at the next meeting. A workforce is being developed in which TB outreach workers receive training in bioterrorism preparedness and response and will be deployed in the event of an emergency.

CDC is making efforts at the federal level to emphasize the importance of TB and increase awareness about this public health issue. The need to "put a face on TB" was one of the most common themes that emerged from focus groups CDC convened throughout the country in collaboration with community leaders. In response to this input, CDC issued three task orders to develop TB educational materials targeted to Hispanic service organizations, healthcare providers of foreign-born persons, and African Americans in the Southeast and their providers. CDC is currently creating a project with a variety of partners to develop medical school and nursing school curricula; TB will be included in the materials. CDC has now published and distributed the second edition of *The TB Challenge: Partnering to Eliminate TB in African Americans* newsletter.

HRSA's most significant priority at this time is to respond to the President's Health Center Initiative to expand access sites by 1,200 and increase the number of patients seen in CHCs by six million by 2006. Dollars appropriated by Congress to HRSA for the initiative can only be used for this purpose. To meet the mandate, HRSA is undergoing a major reorganization in which management of CHCs will become centralized.

HRSA expects CHCs to appropriately screen patients for TB, but this policy is not routinely practiced due to lack of awareness about TB among providers, an insufficient number of outreach workers for follow-up or other reasons. Although HRSA has no

dedicated funds for TB, actions that do not require significant resources can still be taken. For example, TB patients can be missed or not followed because CHCs, community agencies and health departments in the same area may not communicate. A collaborative project could be piloted in one of these areas to identify effective strategies to strengthen communication and coordination among community partners. The pilot project could then be replicated at the national level.

The Substance Abuse and Mental Health Services Administration (SAMHSA) also has no dedicated TB budget. SAMHSA is only mandated to provide TB services by collaborating with local health departments and referring patients to treatment. Unfortunately, SAMHSA is now exploring the possibility of repealing this authorization.

ACET concluded the deliberations by describing next steps to increase the TB budget, advance the TB elimination effort and increase awareness of TB. ACET will make efforts to outreach to, more effectively communicate with and engage new partners. ACET will particularly target HRSA in an ongoing effort to include TB on the health disparities list under the new President's Health Center Initiative. Dr. Kawamura will write letters to the following persons on behalf of ACET: the CDC Director with a copy to the HHS Secretary; Dr. Elizabeth Duke, the HRSA Administrator; Dr. Richard Carmona, the U.S. Surgeon General; and the HHS Health Disparities Council Co-Chairs, Dr. Christina Beato, the Acting Assistant Secretary for Health and Dr. Garth Graham, a White House Fellow.

The discussion also resulted in an **action item**. CDC will compile and provide ACET with information on the TB communication and outreach projects that resulted from the focus groups. The materials should particularly identify the Hispanic service organizations and healthcare providers of foreign-born persons that will receive the TB educational materials. This approach will allow members to initiate further outreach efforts at the local level.

Updates were provided on outstanding agenda items. Dr. Kawamura previously wrote a letter to the HHS Secretary on behalf of ACET to emphasize DTBE's severely inadequate TB budget and underscore the inability of programs to implement TB elimination strategies with insufficient funding. In contacting the HHS Secretary's office, CDC learned that ACET's letter was received and a response is being written.

NCHSTP summarized comments from Dr. Walter Williams, the OMH Director, in response to ACET's questions about the future of OMH. CDC maintains a complete commitment to retain and will not dissolve OMH. Several options are now being explored and discussed in an effort to strengthen the role of OMH. Current activities may be broadened beyond racial, ethnic and minority groups to include health equity issues related to gender, disability and other health disparities. OMH may be housed in

the new Office of Strategy and Innovation in the reorganization to strengthen its impact on all programs throughout CDC. The new organizational structure is still being finalized, but a commitment has been made to maintain OMH in the CDC Director's office. CDC will seek external input on these and other options that are currently being considered for OMH. DTBE will ensure that ACET is provided an opportunity to respond. CDC plans to make a public statement in the next two days to dispel inaccurate rumors about the dissolution of OMH.

Update on Post-Detention Continuity of TB Therapy for U.S. Immigration and Customs Enforcement (ICE) Detainees

Dr. Geralyn Johnson of DIHS presented the status report on behalf of Dr. Diana Schneider, the ACET *ex officio* member for DIHS. DIHS is a division of HRSA that was established with a mission to provide medical services to support ICE's enforcement of immigration laws. DIHS is now detailed to the Department of Homeland Security. In 1994, DIHS's only TB activity was to screen for symptoms, but a state-of-the-art TB program with digital x-ray systems has since been developed. However, the comprehensive screening program resulted in the need to treat TB in an extremely transient population. The average length of stay of ICE detainees is 28 days, but some persons are deported within 24 hours. Over the past ten years, DIHS made strong efforts to resolve this problem with ACET's valuable assistance and guidance.

DIHS is now pleased to announce that a letter from the Acting Director of the ICE Office of Detention and Removal Operations (DRO) was signed and distributed on May 14, 2004 to field personnel with responsibility for detention of illegal aliens. The letter describes ICE's new process for adult detainees diagnosed with active TB to receive continued care. Key language from the letter is outlined as follows. DRO will no longer remove or release any alien from custody with suspected or confirmed active TB without prior consultation with DIHS or the U.S. Public Health Service. Consultations will be held to share preliminary medical and custody information; advise field staff of the detainee's TB care and treatment; complete mandatory notifications and reports; request field approval of a medical hold; and arrange for persons with a final order of deportation to receive continued care. The letter was distributed to ACET for review.

DIHS recognizes that the new directive does not extend to contract jails. Of 22,000 persons ICE detains on a daily basis, 16,000 are detained in contract jails and 6,000 are detained in ICE centers. DIHS must depend on contract jails to report TB or other infectious diseases to local and county health departments because no legal authority exists to enforce these communications. To address this issue, DIHS will continue to solicit guidance from ACET and will also reconvene the CDC/DIHS/ICE workgroup. The

members will be charged with identifying mechanisms to implement the new policy in contract jails; developing evaluation and monitoring criteria; and examining federal and state legal authorities that can be used to achieve treatment compliance through detention or other restrictions.

ACET and CDC made several suggestions for DIHS to consider in resolving issues with contract jails. Contracts between ICE and jails should contain explicit language for diagnosed TB cases to be transferred to ICE service processing centers and monitored by DIHS. TB controllers should be notified of contract jails in their states to enhance coordination and communication between the two groups and assist jails in reporting cases. This effort could be accomplished by DTBE and DIHS jointly developing and distributing a "Dear Colleague" letter to TB controllers throughout the country. To support DIHS's efforts, CDC should include an "ICE Detainee" section in its updated correctional statement that will soon be published. This sub-population is typically ignored in published guidance on TB and other public health issues.

ACET, Dr. Schneider and Dr. Mark Lobato of DTBE were applauded and commended for their contributions and diligent efforts over the past few years that led to the development and approval of the new policy for ICE detainees to receive continued TB care. Agreement was reached for ACET to send a letter to DIHS and ICE in appreciation of developing and approving the new policy. Appropriate CDC, HRSA and HHS officials will be copied on the letter.

Update on the President's Emergency Plan for AIDS Relief (PEPFAR)

Dr. Bess Miller of GAP explained that the President announced the initiative on January 28, 2003. PEPFAR targets 15 countries to prevent seven million new HIV infections; treat two million HIV-infected persons; and provide care for ten million HIV-infected individuals and AIDS orphans. Of the $15 billion that will be allocated to PEPFAR over five years, $10 billion are new dollars, including $1 billion for the Global Fund. PEPFAR's basic legislation authorizes an emergency plan, requires a comprehensive five-year global HIV/AIDS strategy and authorizes a Global AIDS Coordinator (GAC). Mr. Randall Tobias was sworn in as the GAC in October 2003 and was given the rank of Ambassador. He reports directly to the Secretary of State and is responsible for oversight and coordination of all U.S. government resources and international activities to combat the HIV/AIDS pandemic.

Of all PEPFAR funds, 55% will be used for treatment, 20% for prevention, 15% for palliative care, and 10% for orphans and vulnerable children. Of the treatment funds, 75% will be targeted to purchase and distribute ARV drugs. PEPFAR was established as a three-tiered initiative to provide HIV/AIDS leadership in all countries, strong

bilateral HIV/AIDS programs in ~100 countries, and focused attention in 15 countries. PEPFAR's partners include U.S. governmental agencies, host countries, international organizations, the private sector and other donors.

PEPFAR will be implemented as a single U.S. government program in coordination with the GAC, donors and national country plans. HIV prevention, care and treatment services will be integrated under PEPFAR as well. Of PEPFAR's 15 focus countries, 13 have experienced large annual increases in TB incidence since 1997 and eight are among the 22 countries with high TB burdens: Ethiopia, Kenya, Mozambique, Nigeria, South Africa, Tanzania, Uganda and Vietnam. In Botswana, Namibia, South Africa and Zambia, the rate of HIV-positive adults with active TB ranges from 60%-79%. More than 435,000 HIV-infected persons have active TB in the focus countries, but <50% of HIV-positive TB patients were detected and treated under directly observed treatment short-course (DOTS) programs.

TB DOTS programs can contribute to meeting PEPFAR goals by readily identifying candidates for ARV therapy, opportunistic treatment and prevention; serving as a model program for development of ARV programs; providing sites for routine HIV counseling and testing; and making referrals to HIV care and partner testing. These contributions could potentially result in treating or providing care to 19 million persons. Efforts are underway to determine whether PEPFAR funds can be used to support or strengthen TB control through DOTS programs, laboratories, manpower, surveillance, drug resistance, health providers or advocacy.

Several actions will be taken in the future to identify the role of TB in PEPFAR. A TB/HIV surveillance meeting will be convened on June 28-29, 2004. Communication on TB and HIV will be facilitated with the GAC Office. Guidance will be provided to GAP focus country directors and headquarters teams about specific TB/HIV activities to include in FY'05 country operations plans and five-year strategic plans. HIV counseling and testing curricula will be developed for counselors and health providers in TB clinics and other routine counseling and testing clinical settings. CDC staff from GAP and DTBE have been assigned to each of the 15 focus countries to serve as consultants.

Foreign-Born Workgroup Report

Dr. Michael Fleenor, the Workgroup Chair, conveyed that the members represent ACET, BHC, HRSA, NTCA, DTBE, MCN, the American College of Chest Physicians, and state TB controllers. The workgroup determined that the 1998 TB guidelines are not adequate to address the increase of TB in foreign-born persons and updated recommendations should be developed to address emerging foreign-born issues. The workgroup reached this conclusion by soliciting expert opinion, extensively discussing

problems and issues, and prioritizing themes. The workgroup did not recommend a process to address the need and is now seeking ACET's guidance on this issue before proceeding.

The 11 foreign-born themes identified by the workgroup in order of priority are pre- and post-entry management; funding; access to care; current epidemiology; refinement of targeted testing; education of community partners; cost of care; cultural issues related to care; screening of foreign-born persons and their children; standard methods for cross-Border care other than Mexico; and use of BCG vaccination. The workgroup also identified eight new major issues that should be addressed in the updated TB guidelines; the topics are summarized below.

For diagnosis, stronger emphasis should be placed on culture and susceptibility testing rather than AFB smears, pre-screening for MDR-TB prior to U.S. entry, quality assurance in countries of origin, and detection of undocumented cases. For treatment, attention should shift to "blind" treatment of partially treated cases, the quality of domestic follow-up after U.S. arrival, standard methods for cross-Border care, case holding for undocumented cases, and the role of ICE and other correctional facilities in treating undocumented cases.

For contact investigations, an effective strategy should be developed to enhance cross-Border coordination. For screening, gaps should be filled in the areas of targeted testing and LTBI treatment. These uncertainties include the timing and setting where testing should occur, the role of LTBI treatment in primary care, foreign-born persons who are at higher risk and in greater need of LTBI treatment, a redirected focus on LTBI as TB cases decline, LTBI treatment after BCG vaccination, the future rule of QFT, screening children of foreign-born persons, the burden of LTBI in foreign-born persons, and the role of MCN. For funding responsibilities, appropriate authorities that will bear extra costs for MDR-TB, targeted testing and TB control at the Border should be identified.

For surveillance and technical assistance, efforts should be made to improve interaction among local, state and federal levels, enhance program evaluation, and strengthen downstream communication from federal to state and local levels. For community collaboration, linkages should be strengthened with radiologists, pharmacists and other providers who may have contact with foreign-born TB patients. This approach may assist in raising awareness about the need for providers to notify the public health infrastructure of foreign-born TB cases. For other prevention strategies, the role of BCG vaccination in endemic countries should be redefined and new TB vaccines should be developed.

CDC confirmed that the following actions will be taken in response to the workgroup's recommendations. A meeting will be planned and convened in 2005 to review recent data on foreign-born populations, discuss a process to update the 1998 TB guidelines, and develop new recommendations. State refugee health organizations and other key stakeholders will be invited to the meeting. CDC hopes to produce new data before the meeting, particularly TBESC's ongoing evaluation and development of a foreign-born profile.

ACET advised the workgroup to convene a follow-up conference call to inform the full membership about CDC's commitment to hold the foreign-born meeting in 2005. The workgroup will be asked to participate in the planning process for the meeting, but the members will take no further actions until this time. ACET and CDC applauded Dr. Fleenor's outstanding leadership of the workgroup.

HP2010 TB Objective

Mr. Paul Poppe of DTBE announced that CDC is proposing to revise the *HP2010* objective for TB. The current objective of 1 new case/100,000 persons would be changed to a new target of 3 new cases/100,000 persons. The current objective will not be attainable by 2010 due to the following reasons. The average annual rate of decline in TB cases has been ~7.6% over the past ten years, but was only 1.4% in 2003. According to 2003 provisional data, 53% of TB cases are now foreign-born. Level funding also plays a role in the inability to achieve the current objective. The proposed *HP2010* TB objective is consistent with the Government Performance Results Act (GPRA) goal for TB.

While *HP2010* objectives are established for strategic planning purposes and do not result in consequences, GPRA goals are used to hold federal agencies accountable and can lead to reduced funding if targets are not met. CDC has already received opposition from one stakeholder about the proposed goal. Inadequate TB funding could be cited as justification for the inability to reach the current objective of 1/100,000. However, if the proposed target of 3/100,000 is approved, 1/100,000 should be the objective for U.S.-born populations and 20/100,000 should be the target for foreign-born populations. The public comment period for the proposed *HP2010* TB objective will be announced in the *Federal Register* in July 2004.

ACET agreed that the current objective of 1/100,000 is appropriate for the United States and should not be weakened merely to achieve a goal. CDC should be held accountable to its original high standard and leverage funds to meet the goal. In general, ACET suggested that GPRA be broadened to include resources and grantee performance as additional evaluation factors for federal agencies. In particular, ACET

advised CDC to expand the "Justification for Change" to emphasize the tremendous TB budget deficit and discuss the effectiveness of DTBE. For example, DTBE's high PART score can be used to demonstrate that the current objective of 1/100,000 can be achieved with adequate TB resources.

CDC acknowledged the need for further discussion on achievable objectives and realistic goals in light of current resources. In the interim, however, CDC explained that GPRA was established to ensure public dollars are effectively and efficiently utilized. An agency can receive a significantly lower PART score if efforts are made to link funding to program performance and activities. Grantee performance is not a formal component of PART, but is definitely considered during the evaluation.

Several **action items** were noted based on the discussion. CDC will distribute GPRA to ACET and invite policy staff to a future meeting to provide more details. CDC will provide ACET with the *Federal Register* notice announcing the public comment period for the proposed *HP2010* TB objective. CDC will provide ACET with either a written or verbal report on the differences between GPRA and *HP2010*. CDC will schedule the updated NCET federal funding gap report on a future agenda.

Public Comment Period

The Chair opened the floor for public comments; no attendees responded.

Closing Session

The next ACET meeting is tentatively scheduled for October 6-7, 2004; DTBE will poll the members by e-mail to confirm this date. With no further discussion or business brought before ACET, Dr. Kawamura adjourned the meeting at 11:58 a.m. on June 24, 2004.

I hereby certify that to the best of my knowledge, the foregoing Minutes of the proceedings are accurate and complete.

_____
Date

_____
L. Masae Kawamura, M.D.
ACET Chair

ATTACHMENT 1

ACET's June 23, 2004 Motion

ACET should write to the Secretary of Department of Labor, with copies to the Assistant Secretary of Labor for OSHA and the Secretary of Health and Human Services, urgently recommending a delay in enforcement and reassessment of the applicability of the General Industry Respiratory Protection Standard (GIRPS) to occupational exposure to *M. tuberculosis* for the following reasons:

1. CDC is convening a meeting in the near future of key stakeholders, including OSHA, to address respiratory protection issues in the healthcare setting for occupational exposure to patients with TB disease and other potentially infectious agents.

2. Recent scientific data, including studies conducted by NIOSH, strongly suggest that inherent fit characteristics of well-designed respirators may be more important than fit- testing in predicting adequate worker protection.

3. There is a substantial body of evidence suggesting that current prevention and control strategies are effective and therefore, a delay in enforcement will not endanger the health of healthcare workers. TB incidence is at all time low and outbreaks in health care settings have been controlled with implementation of CDC recommendations.

4. The requirements for annual fit testing and medical assessment of the GIRPS are not consistent with both extant and draft CDC guidance.

The Advisory Council for the Elimination of Tuberculosis is seeking a delay in enforcement and reassessment of the applicability of the General Industry Respiratory Protection Standard to occupational exposure to patients with Mycobacterium tuberculosis and other potentially infectious agents.

ATTACHMENT 2

Public Comment

Testimony of Isaac Weisfuse, M.D., M.P.H.
Deputy Commissioner for Disease Control
New York City Department of Health and Mental Hygiene

Regarding the Elimination of Tuberculosis

Before the

Department of Health and Human Services
Advisory Council for the Elimination of Tuberculosis

June 23-24, 2004
Corporate Square, Building 8, 1st Floor Conference Room

Good morning, Chairperson Kawamura, and members of the Advisory Council for the Elimination of Tuberculosis. My name is Dr. Isaac Weisfuse, Deputy Commissioner for Disease Control for the New York City Department of Health and Mental Hygiene (DOHMH). I appreciate this opportunity to submit written testimony on the elimination of TB. We are deeply concerned about the future federal funding to state and local health departments for TB control and elimination activities.

Since its inception in 1866, the New York City DOHMH remains a leader in the fight against TB. The mission of the New York City's DOHMH's Bureau of TB Control is to prevent the spread of TB and eliminate it as a public health problem in the City. Toward this goal, the Bureau conducts multifaceted activities integrating clinical and field services, case management, directly observed therapy (DOT), epidemiology, surveillance, outreach to high risk groups, and education and training of staff, providers and the public. To ensure that treatment for TB meets acceptable standards, the Bureau monitors the care received by every patient diagnosed with active TB in New York City, regardless of whether the patient receives treatment in a DOHMH chest center or elsewhere.

The City's TB rates have been declining since the peak of the recent epidemic in 1992. Despite this recent progress, in 2003 there was an increase in cases for the first time in 10 years. Most of the increase was due to a large increase among the non-U.S. born cases from 700 in 2002 to 771 in 2003. According to preliminary data for 2003, the largest number of cumulative TB cases in non-U.S. born individuals has been among

persons born in China (including the People's Republic of China, Taiwan and Hong Kong), Ecuador, the Dominican Republic, Haiti, India and Mexico. The rise in non-U.S. born TB cases in New York City is related to the ongoing, global TB epidemic. Over one third of the world's population is infected with *Mycobacterium tuberculosis,* while eight to ten million people develop TB and two to three million die of the disease each year. Inadequate treatment of individuals with TB causes further spread of disease and the development of drug resistant tuberculosis.

The national Healthy People 2010 TB case rate goal is 1 case per 100,000 persons. The 2003 Citywide TB case rate of 14.2 cases per 100,000 persons is an increase from 13.5 per 100,000 persons in 2002, the lowest case rate in the City's history. And while the City's TB case rate increased from 2002 to 2003, the *national* TB case rate decreased, from 5.2/100,000 in 2002 to 5.1/100,000 in 2003.

Ensuring that individuals with TB are appropriately treated and cured is the most important method in stopping the spread of TB. Identification and treatment of individuals infected with *M. tuberculosis,* but who do not yet have active TB disease, is also essential in preventing future cases of TB.

The current prevention and control formula for the five-year cycle starting in 2005 indicates large funding reductions to New York City. The total dollar value of federal funds allocated for national TB control and elimination activities has remained static for the last several years while cost of living increases have rapidly reduced the real amount. In the past four years, though funding to the City has been level, there has been a decrease in staffing by 72 positions.

With the reallocation of the national TB funds in 2005, there will be major reductions to NYC. The City's federal portion of the TB control budget will decrease dramatically, by 21%, representing a reduction of approximately $3.5 million. This represents about an 11% reduction in the overall budget for the City's TB control program. This loss will almost completely eliminate targeted testing activities funded by the DOHMH throughout New York City, and will result in 40-50 public health workers losing their jobs. This will markedly decrease the staff for ensuring case management of patients, particularly those high-risk individuals on treatment for latent TB infection (LTBI), and for TB exposure investigations in congregate settings, which are exceptionally resource intensive. These cuts would be particularly damaging because of the high rates of HIV and homelessness in New York, and the potential for rapid spread of TB among these high-risk populations.

In the past three years New York City has made great efforts to improve all aspects of targeted testing activities including targeting the appropriate risk groups, collecting data in the requested format as per CDC guidelines, and improving case management of

patients on latent TB infection (LTBI) treatment. Completion rates have improved in the past year, and the solution to successful prevention is seen in the number of truly high-risk people who are completing treatment. New York City has been focusing on the positive tuberculin skin tests (TST) and HIV positive contacts, and other medical risk groups, as well as recent immigrants who are TST positive.

To remove all specific funding for targeted testing will slow and possibly reverse the progress New York City has made in the last few years. Moreover, DOHMH currently funds various medical providers and community based organizations (CBOs) to reach the immigrant groups with the greatest number of TB disease cases (Chinese, Haitians, Mexicans, Dominicans, and Central Americans) through targeted testing funds. CBOs have the ability to reach the high- risk community, and provide TB screening and treatment of LTBI, as well as the necessary follow-up services to ensure the completion of treatment. These contracts will have to be terminated or drastically reduced in 2005. Without these funds, efforts will be significantly curtailed in providing services to LTBI patients, including current program initiatives to enhance treatment completion rates. Most targeted testing in the community will likely need to be stopped and free tuberculin testing and evaluation for LTBI may have to be abandoned and therefore unavailable to many populations.

In 2000, when federal funds were reduced to NYC, the City was able to reduce the impact of that large cut by increasing city tax levy (CTL) dollars to the TB Program. However, the fiscal difficulties of the City in the past several years have effectively eliminated these funds for the TB Program.

With the assistance of CDC, TB Control programs have developed a cadre of TB control professionals at all levels of government who collectively have significantly impacted TB morbidity, thereby reducing the incidence of active TB cases. The national funding level and the reallocation of funds to the local TB programs in 2005 will seriously jeopardize the expertise available to control TB locally and nationally and will not allow us to meet the national Healthy People 2010 goal.

There appears to be a real disconnect between CDC's focus on targeted testing since 2000 and the proposed plan to discontinue funding for these activities. The considerable effort by local programs and the progress made should provide ample justification for continuation of some targeted funds for LTBI activities. If TB elimination is truly the path we want to follow, funding for LTBI activities is essential. This can only be done; it appears, by increasing federal funds for TB control and prevention activities.

Tuberculosis has not been eliminated, but there has been a substantial reduction in morbidity. I urge you not to repeat the same mistakes of the 1970s and 1980s when funds for the disease program were eliminated, but not the disease. I look forward to

hearing from the council regarding our concerns and would be delighted to provide you with more detailed information at a future meeting of the council.

Again, I would like to thank you for the opportunity to comment on the efforts to eliminate TB.